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[0001] The invention relates to a method to the preparation of monodisperse spherical Polykieselsäure particles, some homogeneous and high (fluorescence) coloring material-dense and/or. Color/fluorescence intensity exhibit.

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[0002] For spherical Polykieselsäure particles there is already series of established technical applications. So various types of spherical Polykieselsäure particles in the size range have themselves around 10 mu m as Sorbentien and/or. Support material for chromatographic methods and used separation processes preserved. In the scientific-technologic tool-making and in various arrangements to the control of flow processes frequent monodisperse Polykieselsäure particles with particle diameters in the Nm and mu become m-range used. Silikati nanoparticles are also for various optical applications of interest. In younger time monodisperse spherical Polykieselsäure particles found however also the increased interest other science disciplines and technical postulant. For example such particles in different modifications in the molecular biology can to the isolation and purification of nucleic acids and proteins, in which cell biology for Phagozytose studies, used in the clinical chemistry as component of diagnostic assay, in the biochemistry and the technical chemistry become as solid phases for the study of the Molecular Recognition phenomena and heterogeneous-catalytic processes.

[0003] Those prior art methods to the preparation of monodisperse spherical Polykieselsäure particles are based at present on the works of STÖBER et al. (J. Colloid & interface Sci. 26, 62 (1968); 30, 568 (1969); US 3,634,588) and were developed further only exemplary ones (BOGUSH et al.: J. Colloid & interface Sci. 142, 1 (1991); van BLAADEREN et al.: J. Colloid & interface Sci. 154, 481 (1992); ZHANG et al.: J. Mater. Sci. Lett. 15, 1902 (1996)). UNGER et al. if 3,534,143 describes the preparation of monodisperse in DE OS, to involve unporösen spherical Polykieselsäure particles by controlled growth processes and the possibility Organo (trialkoxy) of silanes into the classical STÖBER process.

[0004] The thus producible monodisperse spherical Polykieselsäure particle are not however for an additional homogeneous coloration and/or a fluorescence marking suitable. General one is the combination of (fluorescence) coloring materials with (A) spherical silicate particles known in the form of mixtures as colored pigments (EP 767,074, US 4,911,830 and US 5,591,787) or as color coating (US 3,930,063). The expressly non specific incorporation of fluorescent Phthalocyaninderivaten is stressed in the patent specification US 5,763,189 among other things also for silicon dioxide particles. Such mixtures from (fluorescence) coloring materials and silicon dioxide particles possess however the common property that them by simple chemical or physical separation methods, for example by the action of extracting agents, into their components separate to become to be able.

[0005] On the other hand there are already numerous particle applications, which run out on a visualization of (sub) in the run Science range microscopic states and procedures and/or require a safe particle detection.

[0006] Thus the instant invention the object was the basis to make monodisperse spherical Polykieselsäure particles accessible the adjustable particle diameters between 0,05 mu m and 10 mu m as well as an homogeneous and high (fluorescence) coloring material-dense and/or. Color/fluorescence intensity exhibit. The surface of the particles according to invention is to become thereby so designed that it is as little as possible porous and that the functional groups or sequences required for predominant biochemical applications become more immediate during or applied after the actual particle formation by conventional substitution or addition reactions or the respective users the possibility has, on the basis of a standardized Oberflächenchemie, even the required functionality to produce. With the filling (fluorescence) of the coloring materials standing for the order special value should become on a large technological uniformity of the particle synthesis according to invention placed.

[0007] This object becomes dissolved by the fact that the particle formation by simultaneous or successive dosage of the Prekursoren Tetraalkoxysilan and terminal silylated (fluorescence) coloring material into the hydrolysis medium, existing from alcohol, ammonia and water, made. That terminal silylated (fluorescence) coloring material the general formula R 1< R> 2< R> 3< SiR> 4< comes> too, in R< 1>, R< 2> and R< 3> same or various are and for halogen atoms, alkyl, aryl, Alkoxy or Silyloxy groups and R< 4> the complex structure Q< 1> Xm-Yn-q< 2> possesses, in which m and n can accept the values zero and 1. Here Q 1< means> an alkyl chain or an heteroanalogous structure with preferably 1 to 20 chain links. X stands for Carbonyl, Oxycarbonyl, Aminocarbonyl in individual cases for a functional sequence, those and/or. Aminothiocarbonyl groups or a Heteroatom for example oxygen, nitrogen or sulphur to mean knows. Y stands for a bifunctional organic sequence with chaining or ring structure, those with Q< 2> in suitable way linked is. It preferably concerns an alkyl unit or substituted and heteroanalogous alkylene groups, those with Q< 2> in each case over a carbon, a nitrogen, an oxygen or a sulphur atom, for example as esters or amide, linked are. It means that the bifunctional sequence Y in R< 4> also for structural elements of hydraulic XY or aminocarbonic acids as well as their ester and amides to stand can. Q< 2> stands in the general formula R< 4> = Q< 1> - Xm-Yn-q< 2> for a fluorophores system or a dye molecule, the structural possibility offers at Y, or if n is same zero at X and/or. if m and n are same zero, at Q< 1> to bind. In order to realize this connection behavior, the structural element Q 2< orders> over or several functional groups, which are the conventional reaction patterns of substitution or addition accessible. It concerns carbonic acid or sulfonic acid groups in individual cases and/or. over their activated derivatives, over nucleophilic remainders, like hydraulic XY, Mercapto or amino group, over structures, which have replaceable halogen atoms, like halogen alkyl, Halogenalkylcarbonyl or halogen acyl radicals, over Epoxysequenzen or analogous systems and/or. around Heterokumulene, like isocyanates or isothiocyanates, or otherwise activated multiple connection systems. It is just as possible, reactive textile coloring materials, z. B. of the Cibacron type, which has reactive Chlortriazinyl substructures, to the structure of the binding sequence in R< 4> to use. For the suitability as chromophores system in Q< 2> structural no limitations are present. After the invention process all common Chromophore can and/or. Fluorophores, like benzoide and chinoide aromatics and hetero aromatics, for example tri aryl methanes, anthraquinones, Chromene, xanthenes, Indole, quinolines, acridines, Phenoxazine, phenothiazines and phenazines, in addition, Azo and Stilbenfarbstoffe, Indigoderivate, Phthalocyanine and other Tetrapyrrolfarbstoffe as well as Polymethine (cyanines) into Polykieselsäure matrix an incorporated become.

[0008] From synthesis-chemical view the structure of the left sequence Q knows< 1> Xm-Yn-q< 2> single or multi-stage performed becomes. It proved as favorable to accomplish the synthesis stages as potting variants. It cannot become excluded that under the kind and number of the functional groups in the involved reactants constitution isomers or linkages of multiple can occur, what however for the goal of the homogeneous particle colouring irrelevant is. Those for the setting up the left sequence Q< 1> Xm-Yn-q< 2> necessary addition and substitution reactions become conducted in solvents, which are compatible with the hydrolysis mixture with the particle formation. In addition count waters, alcohols and ethers and in particular dipolar aprotic Solventien, like acetone, acetonitrile, N, N-dimethylformamide, N-methyl-morpholinoxid or dimethylsulfoxide. In addition, it consists the possibility, first in little

polar solvents to evaporate for example in (halogenated) hydrocarbons to work these solvents and to transfer the residue into one that solvents managing specified. With the fact ensured becomes that for the structure of the left sequence Q< 1> - Xm-Yn-q< 2> also hydrolysis-sensitive reactants and Intermediate at the use to arrive can.

[0009] During the process of the particle formation the terminal silylated (fluorescence) coloring materials of the general formula R know< 1> R< 2> R< 3> SiR< 4> either when isolated chemical compounds become or used as into situ-synthesis products.

[0010] Can be done in the rule the purification and characterization of the terminal silylated (fluorescence) coloring materials themselves as well as without those the required reactive Intermediate, although they are in principle and bottom application of conventional agents and methods possible.

[0011] In order to obtain during the particle formation an homogeneous distribution (fluorescence) of the coloring material, are a tuned reactivity and a suitable ratio of the Prekursoren Tetraalkoxysilan and terminal silylated (fluorescence) coloring material required. Therefore major Prekursoren becomes used, which Methoxy or Ethoxysubstituenten at the silicon has. Depending upon (fluorescence) the coloring material type, its derivatization and the use the Polykieselsäure particle which can be synthesized can vary the ratio of the Prekursoren relative strong and lies usually between 0,01 and 5 mol%.

[0012] After the invention process it can also possible be attained Farbnuancierungen and Mehrfachcolorierungen. In addition several Prekursoren of the general formula R becomes 1 R 2< R> 3< SiR> 4<,><> in the constitution of the linked sequence Q 1 Xm-Yn-q 2< with>< the particle formation> and in the chemical structure of the fluorophoren system and/or. the dye Q< 2> differentiates, simultaneous or successively metered. However as favorable, the number of terminal silylated (fluorescence) coloring materials proved, itself regarding the chemical structure of the fluorophoren system and/or. the dye Q< 2> differentiate to limit to 2 to 3.

[0013] The Copolykondensation between the Prekursoren Tetraalkoxysilan and terminal silylated (fluorescence) coloring material knows standard agitating reactor thermostatisierten in one on 40 DEG C to 70 DEG C performed will. For the preparation small batches it is just as favourable, the particle formation in a thermostatisierten, with 50 min< -1> to 150 min< -1> to make rotary reaction vessel.

[0014] In some cases has itself as meaningful and/or. necessary proved, the hydrolytic Polykondensatiosreaktion beside various Prekursoren other additives to add. So various surfactants micro emulsions can construct as reaction volumes or stabilize particle dispersions. Such stabilizing effects can proceed also from metal salts effective as Peptisatoren. Will with the Copolykondensation the object followed, the Polykieselsäure matrix proportionately by analogous structures, like aluminates or titanates to replace or with other metals endow, this can take place, by additives from the ranges of metal salts, - oxides, - hydroxides and - alkene oxides and/or. Co-ordination connections and free ligands or from this resultant combinations added become. The dosage of additives from projecting portions made independent or in synergistic manner to metal compounds, which can be already component (fluorescence)< of the coloring material component> Q 2, for example with Metallphthalocyaninen or color lacquers.

[0015] The present process offers thus the possibility to manufacture monodisperse Polykieselsäure particles with adjustable diameters between 0,05 mu m and 10 mu m some homogeneous and high (fluorescence) coloring material-dense and/or. Color/fluorescence intensity exhibit. These particles are further characterized by a distinct Sphärizität, small coefficients of variation in the size distribution and a low porosity of the surface. The method is so applied that the Polykieselsäure particle can exhibit a different color status. Such particle types possess in individual cases the subsequent features: Simple colouring, additives multiple colouring, fluorescence in a defined wavelength range, if necessary also outside of the visible region, fluorescence in several defined wavelength ranges as well as coloration and fluorescence. A significant advantage of the production process consists of the fact that the

resultant particles are both in the common buffers as well as in all conventional solvents elutionsstabil. Even with vibrating lasting several hours in N, N-Dimethyl-formamid no significant release at (fluorescence) coloring materials becomes observed

[0016] The Polykieselsäure particle according to invention possess production-determined an hydrophilic surface. This surface can become after known methods other modified. These methods are based in the rule on addition and substitution reactions. So the particle with a reactive mixture can become from chlorosilanes and hexamethyldisilazane or Alkyltrialkoxysilanen an hydrophobic surface generated by conversion. The otherwise possible conversion with a reactive mixture from chlorosilanes and (aminoalkyl) trialkoxysilanen the generation of a surface, which has terminal amino group. The amino group can be for their part again starting point for other reactions for example with carbonyl compounds. The Polykieselsäure particle producible after the present process are thus surface-functional so equipped that user-specific functional groups, sequences, portion-aluminum or macromolecular structures generated to become to be able. Furthermore it is to be equipped possible various types of such Polykieselsäure particles surface-chemical in such a way that they are in form stable dispersions among themselves compatible. In addition, it exists to equip the possibility various types of such Polykieselsäure particles surface-chemical in such a way that they become guided under opposite dipoles or charges, antibodies/antigen structures or other principles of the molecular recognition a targeted aggregation. Therefore it can quite be for various applications from the run Science range from interest to use mixtures of Polykieselsäure particles itself regarding the particle diameter, which color/fluorescence characteristics and surface functionality can differentiate between.

[0017] The invention is to become on the basis the subsequent examples and the data of the table near explained, without being on it limited.

Example 1: Rhodamin dyed Polykieselsäure particle, D = 800 Nm

[0018] 50 mg (1,13. 10< -4> mol) rhodamine B base become with 40 mu l concentrated hydrochloric acid (14.8 mg) and 1 ml H2O at the rotary evaporator to dry evaporated and subsequent with 5 ml CH2Cl2 offset.

[0019] After short ultrasonic treatment in the water bath the solution with 23,3 mg becomes (1,13. 10< -4> mol) of N, N' dicyclohexylcarbodiimide offset and 30 min with room temperature shaken.

[0020] After addition of 20,3 mg (1,13. 10< -4> mol) (3-Aminopropyl) trimethoxysilan becomes other 16 h shaken. Then the reaction mixture becomes filtered and the resultant red Dichlormethan solution for the particle synthesis used.

[0021] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilane (TEOS) in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the rhodamine B-derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by centrifugation with 2,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 2: Aminofluorescein dyed Polykieselsäure particle, D = 800 Nm

[0022] 50 mg (1,44. 10< -4> mol) of 4 ' - Amino fluorescein in 8 ml dimethylformamides become with 52,4 mg (2,12. 10< -4> mol) 3 (triethoxysilyl) propyl isocyanate offset and 2 h with room temperature shaken. The reaction mixture is fultriert and the resultant yellow DMF solution for the particle synthesis used.

[0023] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the Aminofluorescein derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The

particles become by centrifugation with 2,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 3: DAPI dyed Polykieselsäure particle, D = 800 Nm

[0024] 50 mg (1,43. 10< -4> mol) of 4 ', 6-Diamidino-2-phenyl-indol-dihydrochlorid (DAPI) in 8 ml dimethylformamides become with 14,5 mg (1,43. 10< -4> mol) triethylamine and 52.9 mg (2,14. 10< -4> mol) 3 (triethoxysilyl) propyl isocyanate offset and 2 h with room temperature shaken. The reaction mixture becomes filtered and the resultant yellowish green DMF solution for the particle synthesis used.

[0025] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction that is course-dripped 4 ', 6-Diamidino-2-phenyl-indol-dihydrochlorid-Derivat to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by centrifugation with 2,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 4: 4 (1-Pyrenyl) butter-acid-dyed Polykieselsäure particles, 800 Nm

[0026] 50 mg (1,73. 10< -4> mol) of 4 (1-Pyrenyl) butter-acidic offset become with 5 ml Dioxan. After short ultrasonic treatment in the water bath the solution with 35,7 mg becomes (1,73. 10< -4> mol) of N, N' dicyclohexylcarbodiimide offset and 30 min with room temperature shaken.

[0027] After addition of 31 mg (1,73. 10< -4> mol) (3-Aminopropyl) trimethoxysilan becomes other 16 h shaken. After filtration the resultant yellow Dioxan solution for the particle synthesis becomes used

[0028] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the 1-Pyren-buttersäure-Derivat is course-dripped to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by centrifugation with 2,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 5: 7-Methoxy-coumarin-4-essigsäure-gefärbte Polykieselsäure particle. D = 800 Nm

[0029] 50 mg (2,14. 10< -4> mol) of 7-Methoxy-coumarin-4-essigsäure offset become with 4 ml Dioxan. After short ultrasonic treatment in the water bath the solution with 44 mg (2,14 becomes. 10< -4> mol) of N, N' dicyclohexylcarbodiimide offset and 30 min with room temperature shaken. After addition of 38,3 mg (2,14. 10< -4> mol) (3-Aminopropyl) trimethoxysilan becomes other 16 h shaken. It becomes filtered and the resultant red Dioxan solution for the particle synthesis used.

[0030] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the 7-Methoxy-coumarin-4-essigsäure-Derivat is course-dripped to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by centrifugation with 2,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 6: Nile-blue-dyed Polykieselsäure particles, D = 800 Nm

[0031] 50 mg (1,41. 10< -4> mol) Nile blue chloride in 1 ml dimethylformamide become with 54,4 mg (2,2. 10< -4> mol) 3 (triethoxysilyl) propyl isocyanate offset and 2 h with room temperature shaken. The reaction mixture becomes filtered and the resultant blue DMF solution

for the particle synthesis used.

[0032] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the Nile blue derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by centrifugation with 2,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 7: Rhodamin and Aminofluorescein dyed Polykieselsäure particle, D = 800 Nm

[0033] 50 mg (1,13. 10< -4> mol) rhodamine B base (M = 442.56 g/mol) become with 40 mu l concentrated hydrochloric acid (14.8 mg) and 1 ml H2O at the rotary evaporator to dry evaporated and subsequent with 5 ml dimethylformamides offset.

[0034] After short ultrasonic treatment in the water bath the solution with 23,3 mg becomes (1,13. 10< -4> mol) of N, N' dicyclohexylcarbodiimide offset and 30 min with room temperature shaken. After addition of 20,3 mg (1,13. 10< -4> mol) (3-Aminopropyl) trimethoxysilan becomes other 16 h shaken. Then the reaction mixture becomes filtered.

[0035] 50 mg (1,44. 10< -4> mol) of 4 ' - Aminofluorescein in 8 ml dimethylformamides become with 52,4 mg (2,12. 10< -4> mol) 3 (triethoxysilyl) propyl isocyanate offset and 2 h with room temperature shaken. The reaction mixture becomes filtered, with the solution rhodamine of B-derivative of the mixed and for the particle synthesis used.

[0036] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the mixture from Aminofluorescein and rhodamine B-derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by centrifugation with 2,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 8: Rhodamin, Aminofluorescein and DAPI dyed Polykieselsäure particle, D = 800 Nm

[0037] 50 mg (1,43. 10< -4> mol) of 4 ', 6-Diamidino-2-phenyl-indol-dihydrochlorid in 8 ml dimethylformamides become with 14,5 mg (1,43. 10< -4> mol) triethylamine and 52.9 mg (2,14. 10< -4> mol) 3 (triethoxysilyl) propyl isocyanate offset and 2 h with room temperature shaken. The reaction mixture becomes filtered.

[0038] 50 mg (1,13. 10< -4> mol) rhodamine B base become with 40 mu l concentrated hydrochloric acid (14.8 mg) and 1 ml H2O at the rotary evaporator to dry evaporated and subsequent with 5 ml dimethylformamides offset.

[0039] After short ultrasonic treatment in the water bath the solution with 23,3 mg becomes (1,13. 10< -4> mol) of N, N' dicyclohexylcarbodiimide offset and 30 min with room temperature shaken. After addition of 20,3 mg (1, 13. 10< -4> mol) (3-Aminopropyl) trimethoxysilan becomes other 16 h shaken. Then the reaction mixture becomes filtered.

[0040] 50 mg (1,44. 10< -4> mol) of 4 ' - Amino fluorescein in 8 ml dimethylformamides become with 52,4 mg (2,12. 10< -4> mol) 3 (triethoxysilyl) propyl isocyanate offset and 2 h with room temperature shaken. The reaction mixture becomes filtered, with the solutions rhodamine B and DAPI derivative of the mixed and for the particle synthesis used.

[0041] For the particle synthesis 76.6 is thermostatisiert ml ethanol, 13.6 ml ammonia (25%), 20 ml deionized water and 11.2 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the mixture from Aminofluorescein and rhodamine B-derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 11.2 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by centrifugation with 2,000 rpm

successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 9: Rhodamin dyed Polykieselsäure particle, D = 80 Nm

[0042] 50 mg (1,13. 10< -4> mol) rhodamine B base become with 40 mu l concentrated hydrochloric acid (14.8 mg) and 1 ml H2O at the rotary evaporator to dry evaporated and subsequent with 5 ml methylene chloride offset.

[0043] After short ultrasonic treatment in the water bath the solution with 23,3 mg becomes (1,13. 10< -4> mol) of N, N' dicyclohexylcarbodiimide offset and 30 min with room temperature shaken.

[0044] After addition of 20,3 mg (1,13. 10< -4> mol) (3-Aminopropyl) trimethoxysilan becomes other 16 h shaken. Then the reaction mixture becomes filtered and the resultant red Dichlormethan solution for the particle synthesis used.

[0045] For the particle synthesis 181.5 is thermostatisiert ml ethanol, 68 ml ammonia (25%), 301.5 ml deionized water and 56 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the rhodamine B-derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 56 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by ultracentrifugation with 20,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 10: Pyren-1,3,6,8-tetrasulfonsäure-gefärbte Polykieselsäure particle, D = 800 Nm

[0046] 50 mg (8,19. 10< -5> mol) of Pyren-1,3,6,8-tetrasulfonsäure-Tetranatriumsalz-Hydrat beta - Morpholino ethansulfonsäure hydrate (MES) - become buffer offset with 5 ml 0.1 M.

[0047] After short ultrasonic treatment in the water bath the solution with 38,9 mg (2,03 becomes. 10< -4> mol) of 1 (3-Dimethylaminopropyl) - 3-ethyl-carbodiimid-hydrochlorid (EDC) offset and 30 min with room temperature shaken.

[0048] After addition of 32 mg (2,46. 10< -4> mol) of 1,7-Diamino-heptan (M = 130.23 g/mol) in 3 ml 0.1 M MES buffers becomes other 2 h shaken. The solution becomes then in 50 ml isopropyl alcohol transfered, the flaky precipitation by centrifugation separated in 8 ml dimethylformamides dissolved subsequent dried at the air and. After addition of 94,3 mg (3,8. 10< -4> mol = 94.4 mu l) 3 (triethoxysilyl) propyl isocyanate becomes 2 h with room temperature shaken, filtered and the resultant solution for the particle synthesis used.

[0049] For the particle synthesis 181.5 is thermostatisiert ml ethanol, 68 ml ammonia (25%), 301.5 ml deionized water and 56 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the Pyren-1,3,6,8-tetrasulfonsäure-Derivat is course-dripped to the particle suspension. Subsequent ones are course-dripped other 56 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by ultracentrifugation with 20,000 rpm successive with 200 ml ethanol, 200 ml ethanol water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 11: Light-green-dyed Polykieselsäure particles, D = 800 Nm

[0050] 500 mg (6,31. 10< -4> mol) light-green SF offset become yellowish with 10 ml dimethylformamides. After short ultrasonic treatment in the water bath the solution with 130,2 mg (6,31 becomes. 10< -4> mol) of N, N' dicyclohexylcarbodiimide (DCC) offset and 30 min with room temperature shaken.

[0051] After addition of 113,1 mg (6,31. 10< -4> mol) (3-Aminopropyl) triethoxysilan becomes other 16 h shaken. It becomes filtered and the resultant green DMF solution for the particle synthesis used.

[0052] For the particle synthesis 181.5 is thermostatisiert ml ethanol, 68 ml ammonia (25%), 301.5 ml deionized water and 56 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40

DEG C. 10 min after beginning of reaction the light green derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 56 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by ultracentrifugation with 20,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 12: Reactive-red-dyed Polykieselsäure particles, D = 800 Nm

[0053] 50 mg (5,0. 10< -5> mol) of reactive-red (Cibacron Brilliantrot 3B-A) dimethylformamides offset become with 3 ml. After short ultrasonic treatment in the water bath the solution with 9,0 mg (5,0 becomes. 10< -5> mol = 9 mu l) (3-Aminopropyl) triethoxysilan other 16 h shaken. It becomes filtered and the resultant red DMF solution for the particle synthesis used.

[0054] For the particle synthesis 181.5 is thermostatisiert ml ethanol, 68 ml ammonia (25%), 301.5 ml deionized water and 56 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the reactive red derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 56 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by ultracentrifugation with 20,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 13: Calceinblau dyed Polykieselsäure particle, D = 800 Nm

[0055] 50 mg (1,56. 10< -4> mol) of Calceinblau offset become with 8 ml Dioxan. After short ultrasonic treatment in the water bath the solution with 64,2 mg (3,11 becomes. 10< -4> mol) of N, N' dicyclohexylcarbodiimide (DCC) offset and 30 min with room temperature shaken.

[0056] After addition of 55,8 mg (3,11. 10< -4> mol = 54 mu l) (3-Aminopropyl) trimethoxysilan becomes the cloudy solution other 16 h shaken.

[0057] It becomes filtered and the resultant colorless Dioxan solution for the particle synthesis used.

[0058] For the particle synthesis 181.5 is thermostatisiert ml ethanol, 68 ml ammonia (25%), 301.5 ml deionized water and 56 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the Calceinblau derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 56 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by ultracentrifugation with 20,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 14: Ethidiumbromid dyed Polykieselsäure particle, D = 800 Nm

[0059] 50 mg (1,27. 10< -4> mol) ethidium bromide in 3 ml dimethylformamides become with 58,4 mg (2,63. 10< -4> mol) Isophoron diisocyanat offset and 2 h with room temperature shaken. After addition of 47,2 mg (2,63. 10< -4> mol) (3-Aminopropyl) trimethoxysilan becomes other 2 h with room temperature shaken, the reaction mixture filtered and the resultant red DMF solution for the particle synthesis used.

[0060] For the particle synthesis 181.5 is thermostatisiert ml ethanol, 68 ml ammonia (25%), 301.5 ml deionized water and 56 ml tetraethoxysilanes in a rotary 1 l-flask mixed and with 40 DEG C. 10 min after beginning of reaction the Calceinblau derivative is course-dripped to the particle suspension. Subsequent ones are course-dripped other 56 ml TEOS. 60 min after beginning of reaction the developed suspension on room temperature cooled becomes. The particles become by ultracentrifugation with 20,000 rpm successive with 200 ml ethanol, 200 ml ethanol/water (50/50 v/v) and three times with 200 ml entionisiertem water washed.

Example 15: Revision modification-NO-modified Polykieselsäure particles, D = 800 Nm

[0061] 2 g Polykieselsäure particles (from example 1) are mixed into a paste with 2 h with 150 DEG C in the vacuum dewatered and subsequent in 60 ml tetrahydrofuranes. After addition of

40 mu l Diphenyl dichlorsilan becomes the reaction mixture 1 h in a rotary flask with room temperature activated. Then 2 ml (3-Aminopropyl) triethoxysilan added and the reaction mixture in the rotary flask 20 h are thermostatisiert with 50 DEG C.

[0062] The particles are air-dried by centrifugation with 2,000 rpm successive three times with 60 ml tetrahydrofuranes each and twice with 50 each ml diethyl ethers washed and.

Example 16: Maleic acid-derivatized Polykieselsäure particles, D = 800 Nm

[0063] 2 g revision modification-NO-modified Polykieselsäure particles (from example 10) become in 50 ml methylene chloride with 19,6 mg (2. 10< -4> mol) maleic anhydride 12 h with room temperature shaken. Afterwards the particles are air-dried by centrifugation with 2,000 rpm twice with 50 each ml methylene chloride washed and.

Example 17: Citronensäure modified fluorescent Polykieselsäure particles, D = 800 Nm

[0064] 2 g revision modification-NO-modified Polykieselsäure particles (from example 15) are resuspendiert in 20 ml 0.1 M beta - Mor pholino ethansulfonsäure hydrate (MES) - buffer. 20 mg (1,04. 10< -4> mol) of 1 (3-Dimethylaminopropyl) - 3-ethyl-carbodiimid-hydrochlorid (EDC) become with 20 mg (1,04. 10< -4> mol) of citric acid in 5 ml 0.1 M ss-Morpholino-ethansulfonsäure-hydrate (MES) - buffer dissolved and 10 min with 50 DEG C inkubiert. This solution becomes the particle suspension given and 2 h with room temperature shaken. Afterwards the particles are washed and air-dried by centrifugation with 2,000 rpm twice with 50 each ml waters.

Example 18: Trimethylsilyl modified Polykieselsäure particle, D = 800 Nm

[0065] 2 g Polykieselsäure particles (from example 2) are mixed into a paste with 2 h with 150 DEG C in the vacuum dewatered and subsequent in 40 ml tetrahydrofuranes. After addition of 40 mu l Diphenyl dichlorsilan becomes the reaction mixture 1 h in a rotary flask with room temperature activated. Then 2 is thermostatisiert ml hexamethyldisilazane added and the reaction mixture in the rotary flask 20 h with 50 DEG C.

[0066] The particles become by centrifugation with 2,000 rpm successive three times with 60 ml tetrahydrofuranes each and twice with 50 each ml diethyl ethers washed.

Example 19: Glutaraldehyd modified fluorescent Polykieselsäure particles, D = 800 Nm

[0067] 2 g dyed Polykieselsäure particles (from example 2) are resuspendiert into 20 ml waters and with 360 mu l (2,01. 10< -3> mol) of 50% Glutaraldehydlösung 1 h with 50 DEG C shaken. Afterwards the particles are air-dried by centrifugation with 2,000 rpm twice with 50 each ml waters washed and.

Example 20: Phosohat derivatized fluorescent Polykieselsäure particles, D = 800 Nm

[0068] 142 mg (10< -3> mol) of Diphosphorpentoxid to a large extent dissolved become in 30 ml Dioxan. This solution 1 g becomes dyed Polykieselsäure particles (from example 1) given and 2 h with 50 DEG C shaken. After centrifugation with 2,000 rpm very slow bottom vibrating become 20 ml waters the sediment given. After Resuspendieren the particle becomes the wash process still twice repeated.
EMI19.1

EMI20.1

EMI21.1